Guideline Series 84: **MUTAGENICITY**

EPA Reviewer: Irving Mauer, PH.D. Date: 11/09/94
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Toxicology Branch-I (7509C)

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DATA EVALUATION REPORT

STUDY TYPE: *In vivo* mammalian cytogenetics - micronucleus assay in mice

TOX. CHEM. NO.: 253

P.C.CODE: 024002

MRID NUMBER: 429623-02

TEST MATERIAL: Copper 8-Quinolinolate

SYNONYMS: RO 17-0099/000; oxime-copper (copper oxinate)

STUDY NUMBER(S): B-116'890
SPONSOR: (042567) La Quinoleine SA, via U. S. agent, International Regulatory Consulting, Washington, DC

TESTING FACILITY: F. Hoffmann-La Roche , Basel (Switzerland)

TITLE OF REPORT: Micronucleus Test in the Mouse Bone Marrow *in vivo* After Oral Administration of the Fungicide RO 17-0099/000 (Copper 8-Quinolinolate)

AUTHOR(S): A. Châtelat and J. H. Dresp

REPORT ISSUED: October 17, 1990

CONCLUSION(S) - Executive Summary:

Negative for micronucleus induction in bone marrow cells of mice treated once at doses up to 7500 mg/kg, a non-toxic (but limiting) dose.

Classification: ACCEPTABLE

This study does satisfy the requirement for FIFRA Test Guideline 84-2 for *in vivo* cytogenetic mutagenicity data.

A. MATERIALS

1. Test Material: RO 17-0099/000
Description: Olive-green powder
Lot/Batch #: 8293/3
Purity: 98.5% a.i.
Stability of compound: Stable
CAS #: 10380-28-6
Structure: bis (8-quinolinolate) copper [$C_{18}H_{12}CuN_2O_2$]
Solvent used: SSV: 0.5% sodium carboxymethylcellulose, 0.5% benzylethanol, and 0.4% Tween 80 in 0.9% [aqueous] Sodium chloride.

2. Control Materials:

Vehicle/Final volume/Route of administration: SSV, 15 ml/kg, oral

Positive/Final dose(s)/Route of administration: Procarbazine, 50 mg/kg, oral.

3. Test compound administration:
Volume of test substance administered: 15 ml/kg

Route of administration: Oral

Dose levels used: 0, 3750, 7500 mg/kg X 1

4. Test animals:
a. Species: Mouse, Strain: Fullindorf-Moro, Age [not provided]
Weight: male, 40.2g; female 35.5 g
Source: Biological Research Laboratories, Fullindorf (Switzerland)

b. No. animals used per dose: 5 males, 5 females/sampling time

c. Properly maintained? Yes

B. TEST PERFORMANCE

1. Treatment and Sampling Times:
a. Test compound
Dosing: __X__ once _____ twice (24 hr apart)
_____ other:

Sampling (after last dose): _____ 6 hr _____ 12 hr
__X__ 24 hr __X__ 48 hr __X__ 72 hr
_____ other:

b. Negative and/or vehicle control
Dosing: __X__ once _____ twice (24 hr apart)
_____ other:

Sampling (after last dose): _____ 6 hr _____ 12 hr
__X__ 24 hr __X__ 48 hr __X__ 72 hr
_____ other:

c. Positive control
Dosing: __X__ once _____ twice (24 hr apart)
_____ other:

Sampling (after last dose): _____ 6 hr _____ 12 hr
__X__ 24 hr _____ 48 hr _____ 72 hr
_____ other:

2. Tissues and Cells Examined:

__X__ bone marrow _____ other:

No. of polychromatic erythrocytes (PCE) examined per animal: 1000
No. of normochromatic erythrocytes (NCE; more mature RBCs) examined per animal: 1000

3. Details of slide preparation: Conventional cytological smear procedure.

4. Statistical methods: Mann-Whitney U-Test

5. Evaluation Criteria: According to OECD Guideline #474.

C. REPORTED RESULTS

1. Preliminary cytotoxicity assay: [None performed]

2. Micronucleus assay: The frequency of micronucleated PCE was not increased at any dose or sampling time. No cytotoxicity (measured as PCE/NCE ratio) was found at the HDT, 7500 mg/kg.

D. REVIEWER'S DISCUSSION/CONCLUSIONS: The assay was apparently performed with adequate controls and under procedures acknowledged to generate valid results. The negative results, however, are difficult to assess in the absence of

evidence that the test article (or its active metabolites) were absorbed from the g.i. tract, and transported to the target tissue (bone marrow cells) in effective concentrations to produce cytotoxicity, if not a mutagenic effect.

E. Was test performed under GLPs (is a quality assurance statement present)? Yes.

F. Appendix attached: Yes, Data Table.

[NAME OF TECHNICAL] MICRONUCLEUS

3.5 DISK #3:429623.02:MAUER:MB

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DER MRID #429623-02, Copper 8-Quinolinolate

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